Lead poisoning

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Lead poisoning	
Classification and external resources	
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Part of a series on

Toxicology and poison

Toxicology (Forensic) · Toxinology · History of poison

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Poison · Venom · Toxicant (Toxin) · Acceptable daily

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Treatments

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Lead poisoning (also known as **plumbism**, **colica pictonium**, **saturnism**, Devon colic, or **painter's colic**) is a medical condition caused by increased levels of the heavy metal lead in the body. Lead interferes with a variety of body processes and is toxic to many organs and tissues including the heart, bones, intestines, kidneys, and reproductive and nervous systems. It interferes with the development of the nervous system and is therefore particularly toxic to children, causing potentially permanent learning and behavior disorders. Symptoms include abdominal pain, headache, anemia, irritability, and in severe cases seizures, coma, and death.

Routes of exposure to lead include contaminated air, water, soil, food, and consumer products. Occupational exposure is a common cause of lead poisoning in adults. One of the largest threats to children is lead paint that exists in many homes, especially older ones; thus children in older housing with chipping paint are at greater risk. Prevention of lead exposure can range from individual efforts (e.g. removing lead-containing items such as piping or blinds from the home) to nationwide policies (e.g. laws that ban lead in products or reduce allowable levels in water or soil).

Elevated lead in the body can be detected by the presence of changes in blood cells visible with a microscope and dense lines in the bones of children seen on X-ray. However, the main tool for diagnosis is measurement of the blood lead level; different treatments are used depending on this level. The major treatments are removal of the source of lead and chelation therapy (administration of agents that bind lead so it can be excreted).

Humans have been mining and using this heavy metal for thousands of years, poisoning themselves in the process. Although lead poisoning is one of the oldest known work and environmental hazards, the modern understanding of the small amount of lead necessary to cause harm did not come about until the latter half of the 20th century. No safe threshold for lead exposure has been discovered—that is, there is no known amount of lead that is too small to cause the body harm.

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[edit] Classification

Classically, "lead poisoning" or "lead intoxication" has been defined as exposure to high levels of lead typically associated with severe health effects.[1] Poisoning is a pattern of symptoms that occur with toxic effects from mid to high levels of exposure; toxicity is a wider spectrum of effects, including subclinical ones (those that do not cause symptoms).[2] However, professionals often use "lead poisoning" and "lead toxicity" interchangeably, and official sources do not always restrict the use of "lead poisoning" to refer only to symptomatic effects of lead.[2]

The amount of lead in the blood and tissues, as well as the time course of exposure, determine toxicity.[3] Lead poisoning may be acute (from intense exposure of short duration) or chronic (from repeat low-level exposure over a prolonged period), but the latter is much more common.[4] Diagnosis and treatment of lead exposure are based on blood lead level (the amount of lead in the blood), measured in micrograms of lead per deciliter of blood (µg/dL). The US Centers for Disease Control and Prevention and the World Health Organization state that a blood lead level of 10 µg/dL or above is a cause for concern; however, lead may impair development and have harmful health effects even at lower levels, and there is no known safe exposure level.[5][6] Authorities such as the American Academy of Pediatrics define lead poisoning as blood lead levels higher than 10 µg/dL.[7]

Lead forms a variety of compounds and exists in the environment in various forms.[8] Features of poisoning differ depending on whether the agent is an organic compound (one that contains carbon), or an inorganic one.[9] Organic lead poisoning is now very rare, due to the fact that countries across the world have phased out the use of organic lead compounds as gasoline additives, but such compounds are still used in industrial settings.[9] Organic lead compounds, which cross the skin and respiratory tract easily, affect the central nervous system predominantly.[9]

[edit] Signs and symptoms

Lead poisoning can cause a variety of symptoms and signs which vary depending on the individual and the duration of lead exposure.[10][11] Symptoms are nonspecific and may be subtle, and someone with elevated lead levels may have no symptoms.[12] Symptoms usually develop over weeks to months as lead builds up in the body during a chronic exposure, but acute symptoms from brief, intense exposures also occur.[13] Symptoms from exposure to organic lead, which is probably more toxic than inorganic lead due to its lipid solubility, occur rapidly.[14] Poisoning by organic lead compounds has symptoms

predominantly in the central nervous system, such as insomnia, delirium, cognitive deficits, tremor, hallucinations, and convulsions.[9]

Symptoms may be different in adults and children; the main symptoms in adults are headache, abdominal pain, memory loss, kidney failure, male reproductive problems, and weakness, pain, or tingling in the extremities.[15] The classic signs and symptoms in children are loss of appetite, abdominal pain, vomiting, weight loss, constipation, anemia, kidney failure, irritability, lethargy, learning disabilities, and behavior problems.[15] Children may also experience hearing loss, delayed growth, drowsiness, clumsiness, or loss of new abilities, especially speech skills.[12] Symptoms may appear in children at lower blood lead levels than in adults.[16]

Early symptoms of lead poisoning in adults are commonly nonspecific and include depression, loss of appetite, intermittent abdominal pain, nausea, diarrhea, constipation, and muscle pain.[17] Other early signs in adults include malaise, fatigue, decreased libido, and problems with sleep.[10] An unusual taste in the mouth and personality changes are also early signs.[18] In adults, symptoms can occur at levels above 40 µg/dL, but are more likely to occur only above 50–60 µg/dL.[10] Symptoms begin to appear in children generally at around 60 µg/dL.[19] However, the lead levels at which symptoms appear vary widely depending on unknown characteristics of each individual.[20] At blood lead levels between 25 and 60 µg/dL, neuropsychiatric effects such as delayed reaction times, irritability, and difficulty concentrating, as well as slowed motor nerve conduction and headache can occur.[21] Anemia may appear at blood lead levels higher than 50 µg/dL.[17] In adults, Abdominal colic, involving paroxysms of pain, may appear at blood lead levels greater than 80 µg/dL.[11] Signs that occur in adults at blood lead levels exceeding 100 µg/dL include wrist drop and foot drop, and signs of encephalopathy (a condition characterized by brain swelling), such as those that accompany increased pressure within the skull, delirium, coma, seizures, and headache.[22] In children, signs of encephalopathy such as bizarre behavior, discoordination, and apathy occur at lead levels exceeding 70 µg/dL.[22] For both adults and children, it is rare to be asymptomatic if blood lead levels exceed 100 µg/dL.[11]

[edit] Acute poisoning

In acute poisoning, typical neurological signs are pain, muscle weakness, paraesthesia, and, rarely, symptoms associated with encephalitis.[15] Abdominal pain, nausea, vomiting, diarrhea, and constipation are other acute symptoms.[23] Lead's effects on the mouth include astringency and a metallic taste.[23] Gastrointestinal problems, such as constipation, diarrhea, poor appetite, or weight loss, are common in acute poisoning. Absorption of large amounts of lead over a short time can cause shock (insufficient fluid in the circulatory system) due to loss of water from the gastrointestinal tract.[23] Hemolysis (the rupture of red blood cells) due to acute poisoning can cause anemia and hemoglobin in the urine.[23] Damage to kidneys can cause changes in urination such as decreased urine output.[23] People who survive acute poisoning often go on to display symptoms of chronic poisoning.[23]

[edit] Chronic poisoning

Chronic poisoning usually presents with symptoms affecting multiple systems,[9] but is associated with three main types of symptoms: gastrointestinal, neuromuscular, and neurological.[15] Central nervous system and neuromuscular symptoms usually result from intense exposure, while gastrointestinal symptoms usually result from exposure over longer periods.[23] Signs of chronic exposure include loss of short-term memory or concentration, depression, nausea, abdominal pain, loss of coordination, and numbness and tingling in the extremities.[18] Fatigue, problems with sleep, headaches, stupor, slurred speech, and anemia are also found in chronic lead poisoning.[15] A "lead hue" of the skin with pallor is another feature.[24] A blue line along the gum, with bluish black edging to the teeth is another indication of chronic lead poisoning.[25] Children with chronic poisoning may refuse to play or may have hyperkinetic or aggressive behavior disorders.[15]

[edit] Exposure routes

Lead is a common environmental pollutant.[7] Causes of environmental contamination include industrial use of lead, such as is found in plants that process lead-acid batteries or produce lead wire or pipes, and metal recycling and foundries.[26] Children living near facilities that process lead, such as smelters, have been found to have unusually high blood lead levels.[27] In August 2009, parents rioted in China after lead poisoning was found in nearly 2000 children living near zinc and manganese smelters.[28] Lead exposure can occur from contact with lead in air, household dust, soil, water, and commercial products.[5]

[edit] Occupational exposure

Battery recycling workers are at risk for lead exposure.[29] This worker ladles molten lead into billets in a lead-acid battery recovery facility.

In adults, occupational exposure is the main cause of lead poisoning.[19] People can be exposed when working in facilities that produce a variety of lead-containing products; these include radiation shields, ammunition, certain surgical equipment, fetal monitors, plumbing, circuit boards, jet engines, and ceramic glazes.[18] In addition, lead miners and smelters, plumbers and fitters, auto mechanics, glass manufacturers, construction workers, battery manufacturers and recyclers, firing range instructors, and plastic

manufacturers are at risk for lead exposure.[27] Other occupations that present lead exposure risks include welding, manufacture of rubber, printing, zinc and copper smelting, processing of ore, combustion of solid waste, and production of paints and pigments.[30] Parents who are exposed to lead in the workplace can bring lead dust home on clothes or skin and expose their children.[30]

[edit] Paint

Some lead compounds are bright colors and are used widely in paints,[31] and lead paint is a major route of lead exposure in children.[32] Deteriorating lead paint can produce dangerous lead levels in household dust and soil.[33] Deteriorating lead paint and lead-containing household dust are the main causes of chronic lead poisoning.[15] Many young children display pica, eating things that are not food. Even a small amount of a lead-containing product such as a paint chip or a sip of glaze can contain tens or hundreds of milligrams of lead.[34] Eating chips of lead paint presents a particular hazard to children, generally producing more severe poisoning than occurs from dust.[35] However, removing lead paint from dwellings, e.g. by sanding or torching, can create lead-containing dust and fumes.[36] Therefore, special precautions must be taken when removing lead paint.[36]

[edit] Soil

A lead warning on a gas pump. Tetraethyl lead, which used to be added to gasoline, contributed to soil contamination.

Residual lead in soil contributes to lead exposure in urban areas.[2] Lead content in soil may be caused by broken-down lead paint, residues from lead-containing gasoline or pesticides used in the past, contaminated landfills, or from nearby industries such as foundries or smelters.[37] Although leaded soil is less of a problem in countries that no longer have leaded gasoline, it remains prevalent, raising concerns about the safety of urban agriculture;[38] eating food grown in contaminated soil can present a lead hazard.[39]

[edit] Water

Lead from the atmosphere or soil can end up in groundwater and surface water.[40] It is also potentially in drinking water, e.g. from plumbing and fixtures that are either made of lead or have lead solder.[35][41] Since acidic water breaks down lead in plumbing more

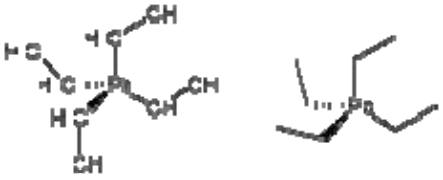
readily, chemicals can be added to municipal water to increase the pH and thus reduce the corrosivity of the public water supply.[35] Chloramines, which were adopted as a substitute for chlorine disinfectants due to fewer health concerns, increase corrosivity.[42] In the US, 14–20% of total lead exposure is attributed to drinking water.[42] In 2004, a team of seven reporters from *The Washington Post* discovered high levels of lead in the drinking water in Washington, D.C. and won an award for investigative reporting for a series of articles about this contamination.[43][44]

In Australia, collecting rainwater from roof runoff used as potable water may contain lead if there are lead contaminates on the roof or in the storage tank.[5] The Australian Drinking Water Guidelines allow a maximum of .01 mg/L lead in water.[5]

[edit] Lead-containing products

Lead can be found in products such as kohl, a South Asian cosmetic, and from some toys.[2] In 2007, millions of toys made in China were recalled from multiple countries due to safety hazards including lead paint.[45] Vinyl mini-blinds, found especially in older housing, may contain lead.[7] Lead is commonly incorporated into herbal remedies such as Indian Ayurvedic preparations and remedies of Chinese origin.[5][10][18] There are also risks of elevated blood lead levels caused by folk remedies like *azarcon* and *greta*, which each contain about 95% lead.[10] Ingestion of metallic lead, such as small lead fishing lures, increases blood lead levels and can be fatal.[46][47][48][49] Ingestion of lead-contaminated food is also a threat. Ceramic glaze often contains lead, and dishes that have been improperly fired can leach the metal into food, potentially causing severe poisoning.[50] In some places, the solder in cans used for food contains lead.[18] People who eat animals hunted with lead bullets may be at risk for lead exposure.[51] Bullets lodged in the body rarely cause significant levels of lead poisoning,[52][53] but bullets lodged in the joints are the exception, as they deteriorate and release lead into the body over time.[54]

[edit] Pathophysiology



Tetra-ethyl lead, still used as an additive in some fuels, can be absorbed through the skin.[18]

Exposure occurs through inhalation, ingestion or occasionally skin contact. Lead may be taken in through direct contact with mouth, nose, and eyes (mucous membranes), and through breaks in the skin. Tetra-ethyl lead, which was a gasoline additive and is still used in fuels such as aviation fuel, passes through the skin; however inorganic lead found in paint, food, and most lead-containing consumer products is only minimally absorbed

through the skin.[18] The main sources of absorption of inorganic lead are from ingestion and inhalation.[17] In adults, about 35–40% of inhaled lead dust is deposited in the lungs, and about 95% of that goes into the bloodstream.[17] Of ingested inorganic lead, about 15% is absorbed, but this percentage is higher in children, pregnant women, and people with deficiencies of calcium, zinc, or iron.[10] Children and infants may absorb about 50% of ingested lead, but little is known about absorption rates in children.[55]

The main body compartments that store lead are the blood, soft tissues, and bone; the half-life of lead in these tissues is measured in weeks for blood, months for soft tissues, and years for bone.[10] Lead in the bones, teeth, hair and nails is bound tightly and not available to other tissues, and is generally thought not to be harmful.[56] In adults, 94% of absorbed lead is deposited in the bones and teeth, but children only store 70% in this manner, a fact which may partially account for the more serious health impacts on children.[6] The estimated half-life of lead in bone is 20–30 years, and bone can introduce lead into the bloodstream long after the initial exposure is gone.[18] The half-life of lead in the blood in men is about 40 days, but it may be longer in children and pregnant women, whose bones are undergoing remodeling, which allows the lead to be continuously re-introduced into the bloodstream.[6] Also, if lead exposure takes place over years, clearance is much slower, partly due to the re-release of lead from bone.[57] Many other tissues store lead, but those with the highest concentrations (other than blood, bone, and teeth) are the brain, spleen, kidneys, liver, and lungs.[13] It is removed from the body very slowly, mainly through urine.[3] Smaller amounts of lead are also eliminated through the feces, and very small amounts in hair, nails, and sweat.[58]

Lead has no known physiologically relevant role in the body,[26][59] and its harmful effects are myriad. Lead and other heavy metals create reactive radicals which damage cell structures including DNA and cell membranes.[60] Lead also interferes with DNA transcription, enzymes that help in the synthesis of vitamin D, and enzymes that maintain the integrity of the cell membrane.[13] Anemia may result when the cell membranes of red blood cells become more fragile as the result of damage to their membranes.[61] Lead interferes with metabolism of bones and teeth[62] and alters the permeability of blood vessels and collagen synthesis.[19] Lead may also be harmful to the developing immune system, causing production of excessive inflammatory proteins; this mechanism may mean that lead exposure is a risk factor for asthma in children.[62] Lead exposure has also been associated with a decrease in activity of immune cells such as polymorphonuclear leukocytes.[62] Lead also interferes with the normal metabolism of calcium in cells and causes it to build up within them.[35]

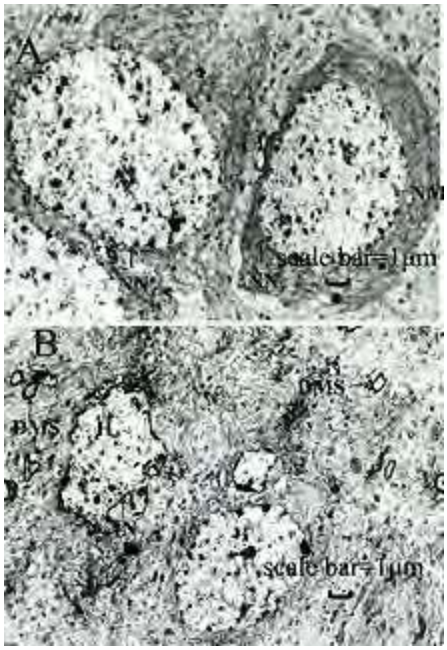
[edit] Enzymes

The primary cause of lead's toxicity is its interference with a variety of enzymes due to the fact that it binds to sulfhydryl groups found on many enzymes.[3] Part of lead's toxicity results from its ability to mimic other metals that take part in biological processes, which act as cofactors in many enzymatic reactions, displacing them at the enzymes on which they act.[13] Lead is able to bind to and interact with many of the same enzymes as these metals but, due to its differing chemistry, does not properly function as

a cofactor, thus interfering with the enzyme's ability to catalyze its normal reaction or reactions. Among the essential metals with which lead interacts are calcium, iron, and zinc.[58]

One of the main causes for the pathology of lead is that it interferes with the activity an essential enzyme called delta-aminolevulinic acid dehydratase, or ALAD, which is important in the biosynthesis of heme, the cofactor found in hemoglobin.[18] Lead also inhibits the enzyme ferrochelatase, another enzyme involved in the formation of heme.[6][18][63] Ferrochelatase catalyzes the joining of protoporphyrin and Fe^{2+} to form heme.[6][13][18] Lead's interference with heme synthesis results in production of zinc protoporphyrin and the development of anemia.[64] Another effect of lead's interference with heme synthesis is the buildup of heme precursors, such as aminolevulinic acid, which may be directly or indirectly harmful to neurons.[65]

[edit] Neurons



Lead exposure damages cells in the hippocampus, a part of the brain involved in memory. Hippocampi of lead-exposed rats (bottom) show structural damage such as irregular nuclei (IN) and denaturation of myelin (DNS) compared to controls (top).[66]

Lead interferes with the release of neurotransmitters, chemicals used by neurons to send signals to other cells.[13][19] It interferes with the release of glutamate, a neurotransmitter important in many functions including learning, by blocking NMDA receptors. The targeting of NMDA receptors is thought to be one of the main causes for lead's toxicity to neurons.[66] A Johns Hopkins report found that in addition to inhibiting the NMDA receptor, lead exposure decreased the amount of the gene for the receptor in part of the brain.[67] In addition, lead has been found in animal studies to cause programmed cell death in brain cells.[19]

[edit] Complications

Lead affects every one of the body's organ systems, especially the nervous system, but also the bones and teeth, the kidneys, and the cardiovascular, immune, and reproductive systems.[59] Hearing loss and tooth decay have been linked to lead exposure,[68] as have cataracts.[69] Intrauterine and neonatal lead exposure promote tooth decay.[70][71][72][73][74][75][76] Aside from the developmental effects unique to young children, the health effects experienced by adults are similar to those in children, although the thresholds are generally higher.[77]

[edit] Renal system

Kidney damage occurs with exposure to high levels of lead, and evidence suggests that lower levels can damage kidneys as well.[78] The toxic effect of lead causes nephropathy and may cause Fanconi syndrome, in which the proximal tubular function of the kidney is impaired.[79] Long-term exposure at levels lower than those that cause lead nephropathy have also been reported as nephrotoxic in patients from developed countries that had chronic kidney disease or were at risk because of hypertension or diabetes mellitus.[80] Lead poisoning inhibits excretion of the waste product urate and causes a predisposition for gout, in which urate builds up.[81][82][83] This condition is known as *saturnine gout*.

[edit] Cardiovascular system

Evidence suggests lead exposure is associated with high blood pressure, and studies have also found connections between lead exposure and coronary heart disease, heart rate variability, and death from stroke, but this evidence is more limited.[84] People who have been exposed to higher concentrations of lead may be at a higher risk for cardiac autonomic dysfunction on days when ozone and fine particles are higher.[85]

[edit] Reproductive system

Lead affects both the male and female reproductive systems. In men, when blood lead levels exceed 40 µg/dL, sperm count is reduced and changes occur in volume of sperm, their motility, and their morphology.[86] A pregnant woman's elevated blood lead level can lead to miscarriage, prematurity, low birth weight, and problems with development during childhood.[87] Lead is able to pass through the placenta and into breast milk, and blood lead levels in mothers and infants are usually similar.[13] A fetus may be poisoned *in utero* if lead from the mother's bones is subsequently mobilized by the changes in metabolism due to pregnancy; increased calcium intake in pregnancy may help mitigate this phenomenon.[88]

[edit] Nervous system

Lead affects the peripheral nervous system (especially motor nerves) and the central nervous system.[13] Peripheral nervous system effects are more prominent in adults and

central nervous system effects are more prominent in children.[20] Lead causes the axons of nerve cells to degenerate and lose their myelin coats.[13]

The brains of adults who were exposed to lead as children show decreased volume, especially in the prefrontal cortex, on MRI. Areas of volume loss are shown in color over a template of a normal brain.[89]

The brain is the organ most sensitive to lead exposure.[89] Lead poisoning interferes with the normal development of a child's brain and nervous system; therefore children are at greater risk of lead neurotoxicity than adults are.[90] In a child's developing brain, lead interferes with synapse formation in the cerebral cortex, neurochemical development (including that of neurotransmitters), and organization of ion channels.[64] It causes loss of neurons' myelin sheaths, reduces numbers of neurons, interferes with neurotransmission, and decreases neuronal growth.[3]

Lead exposure in young children has been linked to learning disabilities,[91] and children with blood lead concentrations greater than 10 µg/dL are in danger of developmental disabilities.[23] Increased blood lead level in children has been correlated with decreases in intelligence, nonverbal reasoning, short-term memory, attention, reading and arithmetic ability, fine motor skills, emotional regulation, and social engagement.[87] The effect of lead on children's cognitive abilities takes place at very low levels.[68][87][92] There is apparently no lower threshold to the dose-response relationship (unlike other heavy metals such as mercury).[93] Reduced academic performance has been associated with lead exposure even at blood lead levels lower than 5 µg/dL.[94][95] Blood lead levels

below 10 µg/dL have been reported to be associated with lower IQ and behavior problems such as aggression, in proportion with blood lead levels.[2] Between the blood lead levels of 5 and 35 µg/dL, an IQ decrease of 2–4 points for each µg/dL increase is reported in children.[23]

high blood lead levels in adults are also associated with decreases in cognitive performance and with psychiatric symptoms such as depression and anxiety.[96] It was found in a large group of current and former inorganic lead workers in Korea that blood lead levels in the range of 20–50 µg/dL were correlated with neuro-cognitive defects.[97] Increases in blood lead levels from about 50 to about 100 µg/dL in adults have been found to be associated with persistent, and possibly permanent, impairment of central nervous system function.[78]

Lead exposure in children is also correlated with neuropsychiatric disorders such as attention deficit hyperactivity disorder and antisocial behavior.[92] Elevated lead levels in children are correlated with higher scores on aggression and delinquency measures.[19] A correlation has also been found between prenatal and early childhood lead exposure and violent crime in adulthood.[87] Countries with the highest air lead levels have also been found to have the highest murder rates, after adjusting for confounding factors.[19] A May 2000 study by economic consultant Rick Nevin theorizes that lead exposure explains 65% to 90% of the variation in violent crime rates in the US.[98][99] A 2007 paper by the same author claims to show a strong association between preschool blood lead and subsequent crime rate trends over several decades across nine countries.[100][101]

[edit] Diagnosis

Diagnosis includes determining the clinical signs and the medical history, with inquiry into possible routes of exposure.[102] Clinical toxicologists, medical specialists in the area of poisoning, may be involved in diagnosis and treatment. The main tool in diagnosing and assessing the severity of lead poisoning is laboratory analysis of the blood lead level (BLL).[12]

Basophilic stippling (arrows) of red blood cells in a 53-year-old who had elevated blood lead levels due to drinking repeatedly from glasses decorated with lead paint.[103]

Blood film examination may reveal basophilic stippling of red blood cells (dots in red blood cells visible through a microscope), as well as the changes normally associated with iron-deficiency anemia (microcytosis and hypochromasia).[18][79] However,

basophilic stippling is also seen in unrelated conditions, such as megaloblastic anemia caused by vitamin B12 (colbalamin) and folate deficiencies.[104]

Exposure to lead also can be evaluated by measuring erythrocyte protoporphyrin (EP) in blood samples.[18] EP is a part of red blood cells known to increase when the amount of lead in the blood is high, with a delay of a few weeks.[11] Thus EP levels in conjunction with blood lead levels can suggest the time period of exposure; if blood lead levels are high but EP is still normal, this finding suggests exposure was recent.[11][21] However, the EP level alone is not sensitive enough to identify elevated blood lead levels below about 35 µg/dL.[18] Due to this higher threshold for detection and the fact that EP levels also increase in iron deficiency, use of this method for detecting lead exposure has decreased.[105]

Blood lead levels are an indicator mainly of recent or current lead exposure, not of total body burden.[106] Lead in bones can be measured noninvasively by X-ray fluorescence; this may be the best measure of cumulative exposure and total body burden.[21] However this method is not widely available and is mainly used for research rather than routine diagnosis.[29] Another radiographic sign of elevated lead levels is the presence of radiodense lines called lead lines at the metaphysis in the long bones of growing children, especially around the knees.[107] These lead lines, caused by increased calcification due to disrupted metabolism in the growing bones, become wider as the duration of lead exposure increases.[107] X-rays may also reveal lead-containing foreign materials such as paint chips in the gastrointestinal tract.[9][107]

Fecal lead content that is measured over the course of a few days may also be an accurate way to estimate the overall amount of childhood lead intake. This form of measurement may serve as a useful way to see the extent of oral lead exposure from all the diet and environmental sources of lead.[108]

Lead poisoning shares symptoms with other conditions and may be easily missed.[23] Conditions that present similarly and must be ruled out in diagnosing lead poisoning include carpal tunnel syndrome, Guillain-Barré syndrome, renal colic, appendicitis, encephalitis in adults, and viral gastroenteritis in children.[102] Other differential diagnoses in children include constipation, abdominal colic, iron deficiency, subdural hematoma, neoplasms of the central nervous system, emotional and behavior disorders, and mental retardation.[12]

[edit] Prevention

Testing kits are commercially available for detecting lead. These swabs, when wiped on a surface, turn pink in the presence of lead.

In most cases, lead poisoning is preventable;[27] the way to prevent it is to prevent exposure to lead.[5] Prevention strategies can be divided into individual (measures taken by a family), preventive medicine (identifying and intervening with high-risk individuals), and public health (reducing risk on a population level).[2]

Recommended steps by individuals to reduce the blood lead levels of children include increasing their frequency of hand washing and their intake of calcium and iron, discouraging them from putting their hands to their mouths, vacuuming frequently, and eliminating the presence of lead-containing objects such as blinds and jewellery in the house.[109] In houses with lead pipes or plumbing solder, these can be replaced.[109] Less permanent but cheaper methods include running water in the morning to flush out the most contaminated water, or adjusting the water's chemistry to prevent corrosion of pipes.[109] Lead testing kits are commercially available for detecting the presence of lead in the household.[50]

Screening is an important method in preventive medicine strategies.[2] Screening programs exist to test the blood of children at high risk for lead exposure, such as those who live near lead-related industries.[12]

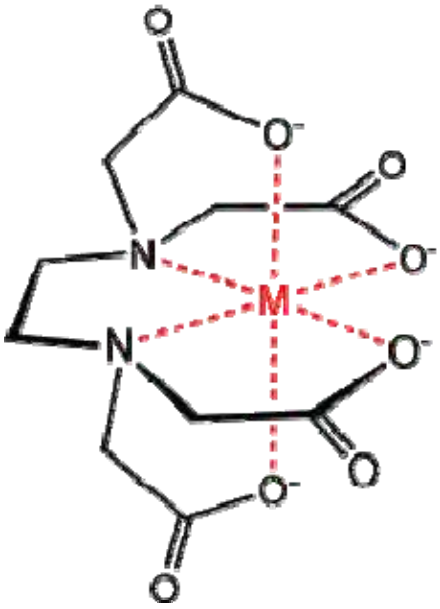
Prevention measures also exist on national and municipal levels. Recommendations by health professionals for lowering childhood exposures include banning the use of lead where it is not essential and strengthening regulations that limit the amount of lead in soil, water, air, household dust, and products.[68] Regulations exist to limit the amount of lead in paint; for example, a 1978 law in the US restricted the lead in paint for residences, furniture, and toys to 0.06% or less.[31] In October 2008, the US Environmental Protection Agency reduced the allowable lead level by a factor of ten to 0.15 micrograms per cubic meter of air, giving states five years to comply with the standards.[110] The European Union's Restriction of Hazardous Substances Directive limits amounts of lead and other toxic substances in electronics and electrical equipment. In some places, remediation programs exist to reduce the presence of lead when it is found to be high, for example in drinking water.[109] As a more radical solution, entire towns located near former lead mines have been "closed" by the government, and the population resettled elsewhere, as was the case with Picher, Oklahoma in 2009.[111][112]

[edit] Treatment

CDC management guidelines for children with elevated blood levels[113]

Blood lead level (µg/dL)	Treatment
10–14	Education, repeat screening
15–19	Repeat screening, case management to abate sources
20–44	Medical evaluation, case management
45–69	Medical evaluation, chelation, case management
>69	Hospitalization, immediate chelation, case management

The mainstays of treatment are removal from the source of lead and, for people who have significantly high blood lead levels or who have symptoms of poisoning, chelation therapy.[114] Treatment of iron, calcium, and zinc deficiencies, which are associated with increased lead absorption, is another part of treatment for lead poisoning.[115] When lead-containing materials are present in the gastrointestinal tract (as evidenced by abdominal X-rays), whole bowel irrigation, cathartics, endoscopy, or even surgical removal may be used to eliminate it from the gut and prevent further exposure.[116] Lead-containing bullets and shrapnel may also present a threat of further exposure and may need to be surgically removed if they are in or near fluid-filled or synovial spaces.[34] If lead encephalopathy is present, anticonvulsants may be given to control seizures, and treatments to control swelling of the brain include corticosteroids and mannitol.[9][117] Treatment of organic lead poisoning involves removing the lead compound from the skin, preventing further exposure, treating seizures, and possibly chelation therapy for people with high blood lead concentrations.[118]



EDTA, a Chelating agent, binds a heavy metal, sequestering it.

A chelating agent is a molecule with at least two negatively charged groups that allow it to form complexes with metal ions with multiple positive charges, such as lead.[119] The chelate that is thus formed is nontoxic[120] and can be excreted in the urine, initially at up to 50 times the normal rate.[65] The chelating agents used for treatment of lead poisoning are edetate disodium calcium ($CaNa_2EDTA$), dimercaprol (BAL), which are injected, and succimer and d-penicillamine, which are administered orally.[121] Chelation therapy is used in cases of acute lead poisoning,[18] severe poisoning, and encephalopathy,[116] and is considered for people with blood lead levels above 25 µg/dL.[23] While the use of chelation for people with symptoms of lead poisoning is widely supported, use in asymptomatic people with high blood lead levels is more controversial.[9] Chelation therapy is of limited value for cases of chronic exposure to low levels of lead.[122] Chelation therapy is usually stopped when symptoms resolve or when blood lead levels return to premorbid levels.[9] When lead exposure has taken place over a long period, blood lead levels may rise after chelation is stopped because lead is leached into blood from stores in the bone;[9] thus repeated treatments are often necessary.[19] Chelating agents can have adverse effects;[29] for example, chelation therapy can lower the body's levels of necessary nutrients like zinc.[120][123] Chelating agents taken orally can increase the body's absorption of lead through the intestine.[124]

Chelation challenge, also known as provocation testing, is used to indicate an elevated and mobilizable body burden of heavy metals including lead.[29] This testing involves collecting urine before and after administering a one-off dose of chelating agent to mobilize heavy metals into the urine.[29] Then urine is analyzed by a laboratory for levels of heavy metals; from this analysis overall body burden is inferred.[125] Chelation challenge mainly measures the burden of lead in soft tissues, and may not accurately reflect long-term exposure or the amount of lead stored in bone.[9] Although the technique has been used to determine whether chelation therapy is indicated and to diagnose heavy

metal exposure, evidence does not support either of these uses because levels after chelation are not comparable to those in the general population.[29]

[edit] Prognosis

Outcome is related to the extent and duration of lead exposure.[126] Effects of lead on the physiology of the kidneys and blood are generally reversible; its effects on the central nervous system are not.[79] While peripheral effects in adults often go away when lead exposure ceases, evidence suggests that most of lead's effects on a child's central nervous system are irreversible.[20] Children with lead poisoning may thus have adverse health, cognitive, and behavioral effects that follow them into adulthood.[37]

Lead encephalopathy is a medical emergency and causes permanent brain damage in 70–80% of children affected by it, even those that receive the best treatment.[12] The mortality rate for people who develop cerebral involvement is about 25%, and of those who survive who had lead encephalopathy symptoms by the time chelation therapy was begun, about 40% have permanent neurological problems such as cerebral palsy.[23]

Exposure to lead may also decrease lifespan and have health effects in the long term.[19] Death rates from a variety of causes have been found to be higher in people with elevated blood lead levels; these include cancer, stroke, and heart disease, and general death rates from all causes.[5] Lead is considered a possible human carcinogen based on evidence from animal studies.[127] Evidence also suggests that age-related mental decline and psychiatric symptoms are correlated with lead exposure.[57] Cumulative exposure over a prolonged period may have a more important effect on some aspects of health than recent exposure.[57] Some health effects, such as high blood pressure, are only significant risks when lead exposure is prolonged (over about one year).[97]

[edit] Epidemiology

Since lead has been used widely for centuries, the effects of exposure are worldwide.[109] Environmental lead is ubiquitous, and everyone has some measurable blood lead level.[10][57] Lead is one of the largest environmental medicine problems in terms of numbers of people exposed and the public health toll it takes.[69] Although regulation reducing lead in products has greatly reduced exposure in the developed world since the 1970s, lead is still allowed in products in many developing countries.[69] In all countries that have banned leaded gasoline, average blood lead levels have fallen sharply.[122] However, some developing countries still allow leaded gasoline,[109] which is the primary source of lead exposure in most developing countries.[91] Poor children in developing countries are at especially high risk for lead poisoning.[91] Of North American children, 7% have blood lead levels above 10 µg/dL, whereas among Central and South American children, the percentage is 33–34%.[109] About one fifth of the world's disease burden from lead poisoning occurs in the Western Pacific, and another fifth is in Southeast Asia.[109]

In developed countries, nonwhite people with low levels of education living in poorer areas are most at risk for elevated lead.[69] In the US, the groups most at risk for lead exposure are the impoverished, city-dwellers, and immigrants.[87] African-American children and those living in old housing have also been found to be at elevated risk for high blood lead levels in the US.[128] Low-income people often live in old housing with lead paint, which may begin to peel, exposing residents to high levels of lead-containing dust.

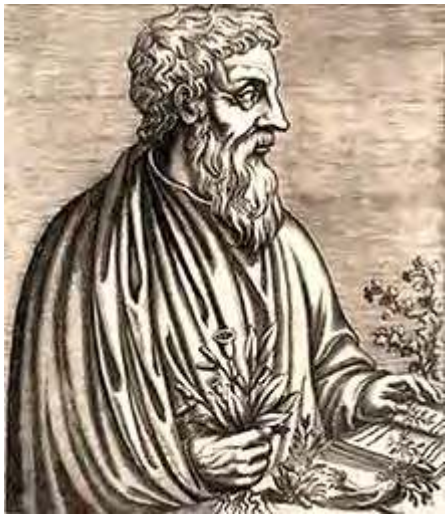
Risk factors for elevated lead exposure include alcohol consumption and smoking (possibly because of contamination of tobacco leaves with lead-containing pesticides).[57] Adults with certain risk factors might be more susceptible to toxicity; these include calcium and iron deficiencies, old age, disease of organs targeted by lead (e.g. the brain, the kidneys), and possibly genetic susceptibility.[97] Differences in vulnerability to lead-induced neurological damage between males and females have also been found, but some studies have found males to be at greater risk, while others have found females to be.[20]

In adults, blood lead levels steadily increase with increasing age.[5] In adults of all ages, men have higher blood lead levels than women do.[5] Children are more sensitive to elevated blood lead levels than adults are.[129] Children may also have a higher intake of lead than adults; they breathe faster and may be more likely to have contact with and ingest soil.[33] Children ages one to three tend to have the highest blood lead levels, possibly because at that age they begin to walk and explore their environment, and they use their mouths in their exploration.[20] Blood levels usually peak at about 18–24 months old.[3] In many countries including the US, household paint and dust are the major route of exposure in children.[33]

[edit] Blood lead reference values

The current reference range for acceptable blood lead concentrations in healthy persons without excessive exposure to environmental sources of lead is less than 10 µg/dL for children and less than 25 µg/dL for adults.[130] The current biological exposure index (a level that should not be exceeded) for lead-exposed workers in the U.S. is 30 µg/dL in a random blood specimen. Blood lead concentrations in poisoning victims have ranged from 30->80 µg/dL in children exposed to lead paint in older houses, 77-104 µg/dL in persons working with pottery glazes, 90-137 µg/dL in individuals consuming contaminated herbal medicines, 109-139 µg/dL in indoor shooting range instructors and as high as 330 µg/dL in those drinking fruit juices from glazed earthenware containers.[131]

[edit] History



Dioscorides noted lead's effect on the mind in the first century A.D.

Roman lead water pipes with taps

Lead poisoning was among the first known and most widely studied work and environmental hazards.[60] One of the first metals to be smelted and used,[31] lead is thought to have been discovered and first mined in Asia Minor around 6500 BC.[32] Its density, workability, and corrosion-resistance were among the metal's attractions.[60]

In the second century B.C. by the Greek botanist Nicander described the colic and paralysis seen in lead-poisoned people.[15][19] Dioscorides, a Greek physician who lived in the first century A.D., wrote that lead makes the mind "give way".[31][132]

Lead was used extensively in ancient Rome from about 500 B.C. to 300 A.D.[32] Julius Caesar's engineer, Vitruvius, reported, "water is much more wholesome from earthenware pipes than from lead pipes. For it seems to be made injurious by lead, because white lead is produced by it, and this is said to be harmful to the human body."[133] Gout, prevalent in affluent Rome, is thought to be the result of lead, or leaded eating and drinking vessels. Sugar of lead (Lead II Acetate) was used to sweeten wine, and the gout that resulted from this was known as saturnine gout.[134] It is even hypothesized that lead poisoning may have contributed to the downfall of Rome.[19][31]

After antiquity, mention of lead poisoning was absent from medical literature until the end of the Middle Ages.[135] In 1656 the German physician Samuel Stockhausen recognized dust and fumes containing lead compounds as the cause of disease, called since ancient Roman times *morbi metallici*, that were known to afflict miners, smelter workers, potters, and others whose work exposed them to the metal.[136][137]

In 17th-century Germany, the physician Eberhard Gockel discovered lead-contaminated wine to be the cause of an epidemic of colic.[136] He had noticed that monks who did not drink wine were healthy, while wine drinkers developed colic,[15] and traced the cause to sugar of lead, made by simmering litharge with vinegar.[136] As a result, Eberhard Ludwig, Duke of Württemberg issued an edict in 1696 banning the adulteration of wines with litharge.[136]

In 18th-century Boston, lead poisoning was fairly frequent on account of the widespread drinking of rum, which was made in stills with a lead component (the "worm").[138] Also in the 18th century, "Devonshire colic" was the name given to the symptoms suffered by people of Devon who drank cider made in presses that were lined with lead.[15] Lead was added to cheap wine illegally in the 18th and early 19th centuries as a sweetener.[139] The composer Beethoven, a heavy wine drinker, suffered elevated lead levels (as later detected in his hair) possibly due to this; the cause of his death is controversial, but lead poisoning is a contender as a factor.[139]

With the Industrial Revolution in the 19th century, lead poisoning became common in the work setting.[31] The introduction of lead paint for residential use in the 19th century increased childhood exposure to lead; for millennia before this, most lead exposure had been occupational.[20] An important step in the understanding of childhood lead poisoning occurred when toxicity in children from lead paint was recognized in Australia in 1897.[31] France, Belgium and Austria banned white-lead interior paints in 1909; the League of Nations followed suit in 1922.[32] However, in the US, laws banning lead house paint were not passed until 1971, and it was phased out and not fully banned until 1978.[32]

The 20th century saw an increase in worldwide lead exposure levels due to the increased widespread use of the metal.[140] Beginning in the 1920s, lead was added to gasoline to improve its combustion; lead from this exhaust persists today in soil and dust in buildings.[5] Blood lead levels worldwide have been declining sharply since the 1980s, when leaded gasoline began to be phased out.[5] In those countries that have banned lead in solder for food and drink cans and have banned leaded gasoline additives, blood lead levels have fallen sharply since the mid-1980s.[141]

The levels found today in most people are orders of magnitude greater than those of pre-industrial times.[18][94] Due to reductions of lead in products and the workplace, acute lead poisoning is rare in most countries today; however, low level lead exposure is still common.[142] It was not until the second half of the 20th century that subclinical lead exposure became understood to be a problem.[135] During the end of the 20th century, the

blood lead levels deemed acceptable steadily declined.[143] Blood lead levels once considered safe are now considered hazardous, with no known safe threshold.[27][144]

[edit] Notable Incidents

15,000 people are being relocated from the Jiyuan in central Henan province to another location. This is the largest lead-smelting center. After 1000 children living around China's largest smelter plant owned by Yuguang Gold and Lead, were found to have excess lead in their blood. The total cost of this project is estimated to around 1 billion yuan ($150 million). 70% of the cost will be paid by local government and the smelter company, while rest be paid by the residents themselves. The government has suspended production at 32 of 35 lead plants.[145] The affected area includes people from 10 different villages.[146]

Arthur Stayner a prominent citizen of Salt Lake City and a father of the sugar beet industry in Utah, died on September 4, 1879 from **lead poisoning** stemming from a lead pellet which became embedded in his heel, causing irritation throughout the day and poisoning his blood.[147]

[edit] In other species

Humans are not alone in suffering from lead's effects; plants and animals are also affected by lead toxicity to varying degrees depending on species.[39] Animals experience many of the same effects of lead exposure as humans do, such as abdominal pain, peripheral neuropathy, and behavioral changes such as increased aggression.[69] Much of what is known about human lead toxicity and its effects is derived from animal studies.[20] Animals are used to test the effects of treatments, such as chelating agents,[148] and to provide information the pathophysiology lead, such as how it is absorbed and distributed in the body.[149]

Farm animals such as cows and horses[150] as well as pet animals are also susceptible to the effects of lead toxicity.[120] Sources of lead exposure in pets can be the same as those that present health threats to humans sharing the environment, such as paint and blinds, and there is sometimes lead in toys made for pets.[120] Lead poisoning in a pet dog may indicate that children in the same household are at increased risk for elevated lead levels.[69]

[edit] Wildlife

Critically endangered California Condor can be poisoned when they eat carcasses of animals shot with lead pellets.

Lead, one of the leading causes of toxicity in waterfowl, has been known to cause die-offs of wild bird populations.[120] When hunters use lead shot, waterfowl such as ducks can ingest the spent pellets later and be poisoned; predators that eat these birds are also at risk.[151] Lead shot-related waterfowl poisonings were first documented in the US in the 1880s.[69] By 1919, the spent lead pellets from waterfowl hunting was positively identified as the source of waterfowl deaths.[152] Lead shot has been banned for hunting waterfowl in several countries,[69] including the US in 1991 and 1997 in Canada.[153] Other threats to wildlife include lead paint, sediment from lead mines and smelters, and lead weights from fishing lines.[153] Lead in some fishing gear has been banned in several countries.[69]

The critically endangered California Condor has also been affected by lead poisoning. As scavengers, condors eat carcasses of game that have been shot but not retrieved, and with them the fragments from lead bullets; this increases their lead levels.[154] Among condors around the Grand Canyon, lead poisoning due to eating lead shot is the most frequently diagnosed cause of death.[154] In an effort to protect this species, in areas designated as the California Condor's range the use of projectiles containing lead has been banned to hunt deer, wild pig, elk, pronghorn antelope, coyotes, ground squirrels, and other non-game wildlife.[155] Also, conservation programs exist which routinely capture condors, check their blood lead levels, and treat cases of poisoning.[154]